AMENDMENT

In the Specification

Please amend the second full paragraph on page 14 as follows:

D1

Another embodiment of the invention comprises a polynucleotide that encodes a 125P5C8-related protein whose sequence is encoded by the cDNA contained in the plasmid deposited with American Type Culture Collection (ATCC; Manassas, VA) as Accession No. ~~[***]~~ PTA-3137 on March 1, 2001. Another embodiment comprises a polynucleotide that hybridizes under stringent hybridization conditions, to the human 125P5C8 cDNA shown in Figure 2 or to a polynucleotide fragment thereof.

Please amend the first full paragraph on page 19 as follows:

D2

As discussed herein, redundancy in the genetic code permits variation in 125P5C8 gene sequences. In particular, it is known in the art that specific host species often have specific codon preferences, and thus one can adapt the disclosed sequence as preferred for a desired host. For example, preferred analog codon sequences typically have rare codons (i.e., codons having a usage frequency of less than about 20% in known sequences of the desired host) replaced with higher frequency codons. Codon preferences for a specific species are calculated, for example, by utilizing codon usage tables available on the ~~INTERNET such as~~ World Wide Web at the http address: ~~http://~~www.dna.affrc.go.jp/~nakamura/codon.html.

Please amend the second and third full paragraphs on page 22 as follows:

D3

Additional illustrative embodiments of the invention disclosed herein include 125P5C8 polypeptides comprising the amino acid residues of one or more of the biological motifs contained within the 125P5C8 polypeptide sequence set forth in Figure 2 or Figure 3. Various motifs are known in the art, and a protein can be evaluated for the presence of such motifs by a number of publicly available sites (see, e.g., http addresses: ~~http://~~pfam.wustl.edu/; ~~http://~~searchlauncher.bcm.tmc.edu/seq-search/struc-predict.html; ~~http://~~psort.ims.u-tokyo.ac.jp/; ~~http://~~www.cbs.dtu.dk/; ~~http://~~www.ebi.ac.uk/interpro/scan.html;

~~http://~~www.expasy.ch/tools/scnpsit1.html; Epimatrix™ and Epimer™, Brown University, ~~http://~~www.brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html; and BIMAS, ~~http://~~bimas.dcrt.nih.gov/.). Motif bearing subsequences of the 125P5C8 protein are set forth and identified in Table XIX.

Table XX sets forth several frequently occurring motifs based on pfam searches (see, e.g., http address: ~~http://~~pfam.wustl.edu/). The columns of Table XX list (1) motif name abbreviation, (2) percent identity found amongst the different member of the motif family, (3) motif name or description and (4) most common function; location information is included if the motif is relevant for location.

Please amend the first full paragraph on page 23 as follows:

In another embodiment, proteins of the invention comprise one or more of the immunoreactive epitopes identified in accordance with art-accepted methods, such as the peptides set forth in Tables V-XVIII. CTL epitopes can be determined using specific algorithms to identify peptides within an 125P5C8 protein that are capable of optimally binding to specified HLA alleles (e.g., Table IV (A) and Table IV (B); Epimatrix™ and Epimer™, Brown University, see e.g., http addresses: ~~http://~~www.brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html; and BIMAS, ~~http://~~bimas.dcrt.nih.gov/. Moreover, processes for identifying peptides that have sufficient binding affinity for HLA molecules and which are correlated with being immunogenic epitopes, are well known in the art, and are carried out without undue experimentation. In addition, processes for identifying peptides that are immunogenic epitopes, are well known in the art, and are carried out without undue experimentation either *in vitro* or *in vivo*.

D4

Please amend the last paragraph on page 24 as follows:

CTL epitopes can be determined using specific algorithms to identify peptides within an 125P5C8 protein that are capable of optimally binding to specified HLA alleles (e.g., Table IV (A) and Table IV (B); Epimatrix™ and Epimer™, Brown University (see e.g., http addresses: ~~http://~~www.brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html); and BIMAS, ~~http://~~bimas.dcrt.nih.gov/). Illustrating this, peptide epitopes from 125P5C8 that are presented in the

D5

context of human MHC class I molecules HLA-A1, A2, A3, A11, A24, B7 and B35 were predicted (Tables V-XVIII). Specifically, the complete amino acid sequence of the 125P5C8 protein was entered into the HLA Peptide Motif Search algorithm found in the Bioinformatics and Molecular Analysis Section (BIMAS) web site listed above. The HLA peptide motif search algorithm was developed by Dr. Ken Parker based on binding of specific peptide sequences in the groove of HLA Class I molecules and specifically HLA-A2 (see, e.g., Falk et al., Nature 351: 290-6 (1991); Hunt et al., Science 255:1261-3 (1992); Parker et al., J. Immunol. 149:3580-7 (1992); Parker et al., J. Immunol. 152:163-75 (1994)). This algorithm allows location and ranking of 8-mer, 9-mer, and 10-mer peptides from a complete protein sequence for predicted binding to HLA-A2 as well as numerous other HLA Class I molecules. Many HLA class I binding peptides are 8-, 9-, 10 or 11-mers. For example, for class I HLA-A2, the epitopes preferably contain a leucine (L) or methionine (M) at position 2 and a valine (V) or leucine (L) at the C-terminus (see, e.g., Parker et al., J. Immunol. 149:3580-7 (1992)). Selected results of 125P5C8 predicted binding peptides are shown in Tables V-XVIII herein. In Tables V-XVIII, the top 50 ranking candidates, 9-mers and 10-mers, for each family member are shown along with their location, the amino acid sequence of each specific peptide, and an estimated binding score. The binding score corresponds to the estimated half-time of dissociation of complexes containing the peptide at 37°C at pH 6.5. Peptides with the highest binding score are predicted to be the most tightly bound to HLA Class I on the cell surface for the greatest period of time and thus represent the best immunogenic targets for T-cell recognition.

Please amend the last full paragraph on page 43 as follows:

D6

Genetic immunization methods can be employed to generate prophylactic or therapeutic humoral and cellular immune responses directed against cancer cells expressing 125P5C8. Constructs comprising DNA encoding a 125P5C8-related protein/immunogen and appropriate regulatory sequences can be injected directly into muscle or skin of an individual, such that the cells of the muscle or skin take-up the construct and express the encoded 125P5C8 protein/immunogen. Alternatively, a vaccine comprises a 125P5C8-related protein. Expression of the 125P5C8-related protein immunogen results in the generation of prophylactic or therapeutic humoral and cellular immunity against cells that bear 125P5C8 protein. Various prophylactic and therapeutic genetic

immunization techniques known in the art can be used (for review, see information and references published ~~at Internet address www.genweb.com~~ on the World Wide Web at "genweb.com").

Please amend the first full paragraph on page 44 as follows:

CTL epitopes can be determined using specific algorithms to identify peptides within 125P5C8 protein that are capable of optimally binding to specified HLA alleles (e.g., Table IV (A) and Table IV (B); Epimer™ and Epimatrix™, Brown University (http address: ~~http://~~www.brown.edu/Research/TB-HIV_Lab/epimatrix/epimatrix.html); and, BIMAS, (http address: ~~http://~~bimas.dcrt.nih.gov/). In a preferred embodiment, the 125P5C8 immunogen contains one or more amino acid sequences identified using one of the pertinent analytical techniques well known in the art, such as the sequences shown in Tables V-XVIII or a peptide of 8, 9, 10 or 11 amino acids specified by an HLA Class I motif (e.g., Table IV (A)) and/or a peptide of at least 9 amino acids that comprises an HLA Class II motif (e.g., Table IV (B)). As is appreciated in the art, the HLA Class I binding grove is essentially closed ended so that peptides of only a particular size range can fit into the groove and be bound, generally HLA Class I epitopes are 8, 9, 10, or 11 amino acids long. In contrast, the HLA Class II binding groove is essentially open ended; therefore a of about 9 or more amino acids can be bound by an HLA Class II molecule. Due to the binding groove differences between HLA Class I and II, HLA Class I motifs are length specific, i.e., position two of a Class I motif is the second amino acid in an amino to carboxyl direction of the peptide. The amino acid positions in a Class II motif are relative only to each other, not the overall peptide, i.e., additional amino acids can be attached to the amino and/or carboxyl termini of a motif-bearing sequence. HLA Class II epitopes are often 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids long, or longer than 25 amino acids.

D7

Please amend the third full paragraph on page 50 as follows:

~~[***]~~ PTA-3137 has been deposited under the requirements of the Budapest Treaty on ~~[***]~~ March 1, 2001 with the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, VA 20110-2209 USA, and has been identified as ATCC Accession No. ~~[***]~~ PTA-3137.

D8

All restrictions on access to these deposits will be irrevocably removed prior to issuance of a patent on the present application or counterpart thereof.

Please amend the fifth full paragraph on page 55 as follows:

D9

The 125P5C8 cDNA was deposited on ~~[***]~~ March 1, 2001 with the American Type Culture Collection (ATCC; Manassas, VA) as plasmid ~~[***]~~ *Escherichia coli* DH5A 125P5C8PRO, and has been assigned Accession No. PTA-~~[***]~~ 3137.

Please amend the last paragraph on page 55 as follows:

D10

The chromosomal localization of 125P5C8 was determined using the NCBI Human Genome web site (available at http address: ~~http://~~www.ncbi.nlm.nih.gov/genome/seq/page.cgi?F=HsBlast.html&&ORG=Hs). The mapping program placed 125P5C8 on chromosome 6q23, between D6S1040 and D6S457, a genomic region found to be rearranged in certain cancers.

Please amend the third full paragraph on page 68 as follows:

D11

The effect of the 125P5C8 protein on tumor cell growth can be evaluated *in vivo* by gene overexpression in tumor-bearing mice. For example, SCID mice can be injected SQ on each flank with 1 x 10^6 of either PC3, TSUPR1, or DU145 cells containing tkNeo empty vector or 125P5C8. At least two strategies may be used: (1) Constitutive 125P5C8 expression under regulation of a promoter such as a constitutive promoter obtained from the genomes of viruses such as polyoma virus, fowlpox virus (UK 2,211,504 published 5 July 1989), adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus and Simian Virus 40 (SV40), or from heterologous mammalian promoters, *e.g.*, the actin promoter or an immunoglobulin promoter, provided such promoters are compatible with the host cell systems. (2) Regulated expression under control of an inducible vector system, such as ecdysone, tet, etc., can be used provided such promoters are compatible with the host cell systems. Tumor volume is then monitored at the appearance of palpable tumors and is followed over time to determine if 125P5C8-expressing cells grow at a faster rate and whether tumors produced by 125P5C8-expressing cells

demonstrate characteristics of altered aggressiveness (e.g. enhanced metastasis, vascularization, reduced responsiveness to chemotherapeutic drugs). Additionally, mice can be implanted with 1 x 10^5 of the same cells orthotopically to determine if 125P5C8 has an effect on local growth in the prostate or on the ability of the cells to metastasize, specifically to lungs, lymph nodes, and bone marrow. Also see Saffran et al, "Anti-PSCA mAbs inhibit tumor growth and metastasis formation and prolong the survival of mice bearing human prostate cancer xenografts" PNAS 10:1073-1078 ~~or www.pnas.org/cgi/doi/10.1073/pnas.051624698~~.

Please amend the first full paragraph on page 69 as follows:

D12

Antibody efficacy on tumor growth and metastasis formation is studied, e.g., in a mouse orthotopic prostate cancer xenograft model. The antibodies can be unconjugated, as discussed in this Example, or can be conjugated to a therapeutic modality, as appreciated in the art. We demonstrate that anti-125P5C8 MAbs inhibit formation of both the androgen-dependent LAPC-9 and androgen-independent PC3-125P5C8 tumor xenografts. Anti-125P5C8 mAbs also retard the growth of established orthotopic tumors and prolonged survival of tumor-bearing mice. These results indicate the utility of anti-125P5C8 mAbs in the treatment of local and advanced stages of prostate cancer. (See, e.g., (Saffran, D., et al., PNAS 10:1073-1078 ~~or www.pnas.org/cgi/doi/10.1073/pnas.051624698~~).

Please amend the third full paragraph on page 70 as follows:

D13

Subcutaneous (s.c.) tumors are generated by injection of 1 x 10^6 LAPC-9, PC3, or PC3-125P5C8 cells mixed at a 1:1 dilution with Matrigel (Collaborative Research) in the right flank of male SCID mice. To test antibody efficacy on tumor formation, i.p. antibody injections are started on the same day as tumor-cell injections. As a control, mice are injected with either purified mouse IgG (ICN) or PBS; or a purified monoclonal antibody that recognizes an irrelevant antigen not expressed in human cells. In preliminary studies, no difference is found between mouse IgG or PBS on tumor growth. Tumor sizes are determined by vernier caliper measurements, and the tumor volume is calculated as length x width x height. Mice with s.c. tumors greater than 1.5 cm in diameter are sacrificed. PSA levels are determined by using a PSA ELISA kit (Anogen,

Mississauga, Ontario). Circulating levels of anti-125P5C8 mAbs are determined by a capture ELISA kit (Bethyl Laboratories, Montgomery, TX). (See, e.g., (Saffran, D., et al., PNAS 10:1073-1078~~ or www.pnas.org/cgi/doi/10.1073/pnas.051624698~~).